

**AMENDMENTS TO THE SPECIFICATION:**

Please replace the first paragraph, added by preliminary amendment, with the following paragraph:

This is a division of Application No. 09/742,361, filed December 22, ~~2003~~ 2000, which is a continuation of International Application No. PCT/EP99/04490, filed June 29, 1999, which in turn is a continuation-in-part of U.S. ~~application~~ Application No. 09/107,383, filed June 30, ~~1998~~ 1998, ~~now~~ which issued as U.S. Patent No. 6,190,667 on February 20, 2001, all of which are incorporated herein by reference.

Please replace the first paragraph on page 4 with the following paragraph, which was previously amended November 25, 2003:

Figure 3A and Figure 3B ~~show~~ shows the alignment of the amino acid sequence of Urel from *H. pylori* with those of similar proteins and prediction of the two-dimensional structure of members of the Urel/AmiS protein family. Residues identical at one position in, at least, four sequences are boxed, and dashes indicate gaps inserted to optimize alignment. The organisms from which the sequences originated and the degree of identity with the *H. pylori* Urel protein are: Urel-Hp, *Helicobacter pylori* (195 residues, accession No. M84338) (SEQ ID NO: 10); Urel-Hf, *Helicobacter felis* (74% identity over 196 residues, accession No. A41012) (SEQ ID NO: 11); Urel-Lacto, *Lactobacillus fermentum* (55% identity over the 46 residues-long partial sequence, accession No. D10605) (SEQ ID NO: 12); Urel-Strepto, *Streptococcus salivarius* (54% identity over the 129 residues-long partial sequence, accession No. U35248) (SEQ ID NO: 13); AmiS-Myco, *Mycobacterium smegmatis* (39% identity over 172 residues,

accession No. X57175) (SEQ ID NO: 14); AmiS-Rhod, *Rhodococcus* sp. R312 (37% identity over 172 residues, accession No. Z46523) (SEQ ID NO: 15) and AmiS-Pseudo, *Pseudomonas aeruginosa* (37% identity over 171 residues, accession No. X77161) (SEQ ID NO: 16). Predicted transmembrane  $\alpha$ -helices are shown as shaded boxes. The regions separating these boxes are hydrophilic loops labeled "IN" when predicted to be intracellular and "OUT" when predicted to be extracellular.

Please replace the first full paragraph at page 15 with the following paragraph:

Alignment of these Urel/AmiS proteins [using the Clustal W(1.60) program] defined strongly conserved stretches of amino acids (Figure 3). All but one of these conserved blocks are in highly hydrophobic segments. These regions, each 17 to 22 residues long, are probably folded into transmembrane  $\alpha$ -helices (Figure 3). Six transmembrane regions were predicted for the proteins from *H. pylori*, *H. felis*, and *P. aeruginosa* and seven for those from *Rhodococcus* sp. R312 and *M. smegmatis* (highly reliable predictions, performed with pHD, a profile fed neural network system as described by Rost et al. (22)). The orientation of the Urel/AmiS proteins in the membrane was deduced from the charges of the intercalated hydrophilic regions, which are short in these proteins (Figure 3). The first five such regions are poorly conserved and of various length. The last interhelical segment common to these proteins is significantly more conserved than the others. This region predicted to be intracellular may be the active site of Urel or a site of multimerization or interaction with an intracellular partner. These results strongly suggest that the members of the Urel/AmiS family, found in both Gram-positive and -negative bacteria, are integral membrane

proteins. These proteins have no signal sequence and should therefore be inserted into the cytoplasmic membrane in Gram-negative bacteria.